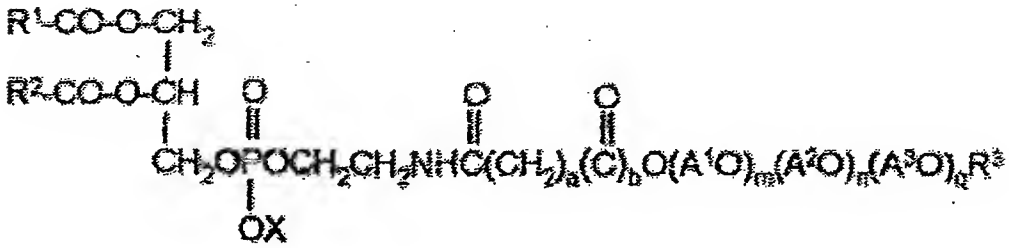
REMARKS/ARGUMENTS

Upon entry of this amendment, claims 1 and 2 will be amended, whereby claims 1-20 will be pending.

The amendment of claims 1 and 2 is being made in accordance with the Examiner's suggestion in the 35 U.S.C. 112, second paragraph rejection, and is supported by Applicants' originally filed application including Applicants' originally filed application and the compounds disclosed therein. For example, attention is directed to Synthesis Examples 1 and 2 beginning at page 19 which comprise compounds including monomethyl-polyoxypropylene/polyoxyethylene-succinyl (molecular weight: 2000)-distearoylphosphatidylethanolamine and monomethyl-polyoxypropylene/polyoxyethylene glutaryl (molecular weight: 2000)-distearoylphosphatidylethanolamine.

Still further, attention is directed to the International Preliminary Examination Report on Patentability a copy of which was submitted with the Information Disclosure Statement filed March 29, 2007. In this Report, it is indicated that the International Preliminary Report on Patentability was carried based on the understanding that formula (I) in the claims is a typographical error for:



Accordingly, for at least the reasons noted above,

Reconsideration and allowance of the application are respectfully requested.

Claim Of Priority

Applicants express appreciation for the acknowledgement of the claim of foreign priority, and receipt of the certified copy. In order that the record is clear, Applicants note that the certified copy of been received in this national stage application.

Consideration Of Information Disclosure Statements

Applicants express appreciation for the inclusion with the Office Action of an initialed copy of the Form PTO-1449 submitted with the Information Disclosure Statement filed March 29, 2007, whereby the Examiner's consideration of the Information Disclosure Statement is of record.

Response To Rejection Under 35 U.S.C. 112, Second Paragraph

In response to the rejection of claims 1-2 [apparently claims 1-20] under 35 U.S.C. 112, second paragraph, as being indefinite, Applicants respectfully submit the following.

The rejection contends that the claims are confusing in reciting "acyl group" for R^1CO and R^2CO groups asserting that it is unclear whether the groups are either ketone or ester functionalities. The Examiner suggests amendment to R^1CO_2 and R^2CO_2.

In response and as discussed above, by the amendment herein the formula has been corrected in the manner indicated by the Examiner. However, Applicants submit

that it is not necessary to change the description of the R^1CO and R^2CO groups when referring to the formula. If the Examiner has any questions in this regard, the Examiner is requested to contact the undersigned to discuss the claim language.

Response To Art Based Rejections

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Von Wronski et al., US 2002/0147136.

In response, Applicants respectfully submit the following.

Von Wronski discloses a composition that targets endothelial cells or tumor cells or other cells that express NP-1 receptor, wherein said composition comprises a compound represented by the formula A-L-B. Preferred examples of the substrate B comprising a lipid are disclosed in paragraph [0127] on page 12, including for example phosphatidylethanolamines (PE) such as dipalmitolylphosphatidylethanolamine (DPPE) and disteraoylphosphatidyl ethanolamine (DSPE) and the like. Von Wronksi teaches that a phospholipid derivative such as N-Glutaroyl-DPPE and a polyoxyethylene derivative can be used in combination for preparation of a liposome. However, the combination is a mere mixture of N-Glutaroyl-DPPE and a polyoxyethylene derivative, except for DPPE-PEG being a pegylated lipid which will be discussed later, and Von Wronski fails to teach nor suggest that the above two kinds of compounds are bound via a covalent bond to form a single chemical compound.

Von Wronksi also teaches that polyoxypropylene glycol, polyoxyethylene glycol or the like can be used as a film forming surfactant (see, paragraph [0146] at page 16).

However, the additive compound as a film forming surfactant is also used as an ingredient of a mixture, and is not covalently bound with a phospholipid derivative.

In addition, Von Wronksi teaches, at paragraph [0152] at page 17, the use of the first surfactant as a hydrophobic phospholipid, and the use of the more hydrophilic second surfactant. Examples of the second surfactant include a block copolymer of polyoxypropylene and polyoxyethylene such as Pluronic F-68. However, Von Wronski neither teaches nor suggests that the first and second surfactants may be covalently bound to each other to form a single chemical compound.

Von Wronski discloses that the compound represented by A-L-B, such as those of formula Ia or IIa, is suitable for forming a lipid membrane (paragraph [0168] at page 18), wherein A is an oligopeptide analogue deriving from TKPPR (Thr-Lys-Pro-Pro-Arg) that binds to a receptor on the surface of cells to impart targeting property, and as a result, the compound of formula Ia or IIa represented by A-L-B is characterized to be capable of targeting endothelial cells or tumor cells that express NP-1. The compounds of the present invention can increase the hydration layer on the surface of lipid membrane structures, including liposomes as typical examples, in order to achieve higher stability in blood to avoid recognition of cells, which is achieved by locating the moiety of the polyalkylene derivative on the surface of a lipid membrane structure. Moreover, the compounds of the present invention are not modified with a targeting molecule such as the oligopeptide A at the end thereof. Accordingly, the presently claimed compounds are structurally distinguishable from the compounds disclosed in Von Wronski. Moreover, as discussed above, Von Wronski is silent about a compound wherein an alkylene oxide

derivative that increases a hydration layer and a phospholipid derivative are covalently bound to each other.

Von Wronski discloses DPPE-PEG being a pegylated lipid as a preferred lipid "B" in the above-noted paragraph [0127]. This type of lipid wherein a homopolymer of polyoxyethylene and a phospholipid are covalently bound is known before the present invention was made (see, Klibanov et al., FEBS Lett., 268, 235, 1990 which has been cited in Applicants Information Disclosure Statement filed March 29, 2007), which lipid was used as a comparative compound in Examples of the specification of the present application.

It is known that a degree of stability of liposome in blood, whose surface is modified with a polyethylene glycol lipid, is correlated with a volume of hydration layer, i.e., a higher volume of the hydration layer gives higher stability of the liposome in blood. For the increase of the hydration layer, studies were focused, before the present invention was made, on increase of molecular weight of polyethylene glycol chain or increase of an amount of a polyethylene glycol lipid in a liposome. According to the present invention, the claimed compound is introduced with an alkylene oxide polymer consisting of $(A^1O)_m(A^2O)_n(A^3O)_q$ wherein the units of alkylene oxides (e.g., propylene oxide or butylene oxide) have different number of carbon atoms, thereby transverse expansion of the alkylene oxide chain is significantly reduced and lengthwise expansion of the alkylene oxide chain is accelerated, and thereby efficient formation of hydration layer on the surface of the liposome is achievable.

Applicants note that the rejection, after discussing the disclosure of Von Wronski, asserts that Ueno et al. is deficient in the sense that it does not explicitly state the ratio of

oxyethylene groups to oxyalkylene groups, the ratio of oxyethylene groups to oxyethylene groups and oxypropylene groups, the weight ratio or the average molar number of the oxyalkylene groups.

Apparently, the rejection intended to refer to Von Wronski when referencing Ueno et al. However, in any event, there is no teaching or suggestion and/or any reason why one having ordinary skill in the art would seek to modify the compounds disclosed by Von Wronski to arrive that the compounds, compositions, lipid membrane structure and/or surfactant recited by Applicants at least for the reasons discussed above. The Examiner is reminded that there must be some direction in the prior art utilized in the rejection to arrive at Applicants' claimed subject matter, and Applicants' disclosure cannot be utilized to support the rejection. If the rejection is maintained, the Examiner is respectfully requested to establish why one having ordinary skill in the art would arrive at the claimed subject matter, including what routine and normal experimentation would be utilized.

Accordingly, the rejection should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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